Final Progress Report

Project Title: TREAT ECARDS: Translating Evidence into Action: Electronic Clinical Decision Support in ARDS

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Abstract:

Purpose: The overall goal of this proposal is to develop and evaluate the effectiveness of a Clinical Decision Support Tool for the identification (ARDS Sniffer 2.0) and management of Acute Respiratory Distress Syndrome (ARDS) (ECARDS: Electronic Clinical decision support in ARDS) to promote uptake of evidence-based practices.

Scope: Acute respiratory failure (ARF) is the most common acute organ dysfunction in US hospitals and ARDS is the most severe form of ARF with mortality of 40%. Only 1/3 of patients with ARDS are recognized, which contributes to under-utilization of practices proven to improve outcomes. For example, low tidal volume ventilation is used in only 13-40% of ARDS patients. To improve the outcomes in ARDS, interventions are needed to overcome the barrier of under-recognition of ARDS and the barrier of clinician under-utilization of Evidence-Based Practices (EBPs) for ARDS.

Methods: A multi-modality approach using mixed methods was adopted. A deep machine learning approach was used to develop and validate a long short term memory model on real world Electronic Health Records (EHR) data for the timely identification of patients with ARDS. EBPs to target for implementation in ARDS was identified through a systematic review, clinician interviews and survey using the Guideline Implementability Appraisal (GLIA) tool. An electronic dashboard and reporter tool (ECARDS) were constructed based upon the data needs and clinical decision making from clinicians and upon EHR-based performance measures (EPMs) that correlate with outcomes.

Results: A long short term memory model (ARDS Sniffer 2.0) was developed from EHR data from 3278 mechanically ventilated (MV) patients admitted to Montefiore Healthcare System in 2017-2018 and validated on 781 MV non-COVID patients and 5672 COVID-19 patients, including 803 MV COVID-19 patients. ARDS Sniffer 2.0 identified ARDS with a sensitivity of 86%, 70% and 92% in non-COVID MV patients, COVID-19 patients with and without MV, and MV COVID-19 patients, respectively. In the MV COVID-19 cohort, the prevalence of ARDS was so high that the Sniffer alerted on 75% of patients, with nearly 100% of patients who triggered the Sniffer confirmed to have ARDS. A systematic review in ARDS and ARF resulted in 20 EBPs. The clinicians and research team responses on the GLIA tool and EHR analysis of measurability of the practices reduced this to 6 EBPs (low tidal volume ventilation, spontaneous awakening trials, spontaneous breathing trials, coordinated breathing and awakening trials, avoidance of coma and avoidance of benzodiazepine use) with validated EPMs that correlate with mortality, duration of MV and ventilator-free days. ARDS Sniffer 2.0 and EPMs were incorporated into an electronic decision support tool (ECARDS) that consist of a real-time dashboard that tracks the severity of illness and likelihood of ARDS, and an ICU Reporter that tracks outcomes and EPMs for each ICU. This tool was created in a simulated sandbox for the research team to test. However, the unprecedented COVID-19 pandemic in 2020 strained the resources and changed the clinical context for ARDS. Whereas before ARDS was under-recognized, the hospital was now filled with patients with COVID-19 pneumonia, and most of them were recognized to have ARDS. Given the resource strain and change in prevalence and recognition of ARDS, the institution decided to hold off on the implementation of ECARDS in the clinical setting.

Key Words: ARDS, electronic clinical decision support, evidence-based practice, machine learning, prediction.

PURPOSE:

The overall goal of this proposal is to develop and evaluate the effectiveness of a CDSS for identification (ARDS Sniffer 2.0) and management of ARDS (**ECARDS**: **E**lectronic **C**linical decision support in **ARDS**) that **TR**anslate **E**vidence into **A**c**T**ion (**TREAT**) by being real-time and patient and context-appropriate.

Specific Aim #1: To develop and validate an automated, EMR-based tool to identify patients with ARDS or high risk of hospital mortality.

Specific Aim #2: To develop an evidence-based, context-appropriate, Electronic Clinical decision support system in ARDS (ECARDS) for the management of ARDS.

Specific Aim #3: To evaluate the effectiveness of the ARDS Sniffer 2.0 and ECARDS in a real world clinical setting.

Specific Aim #4: To promote the dissemination of the ARDS Sniffer 2.0 and ECARDS through our partner professional organizations

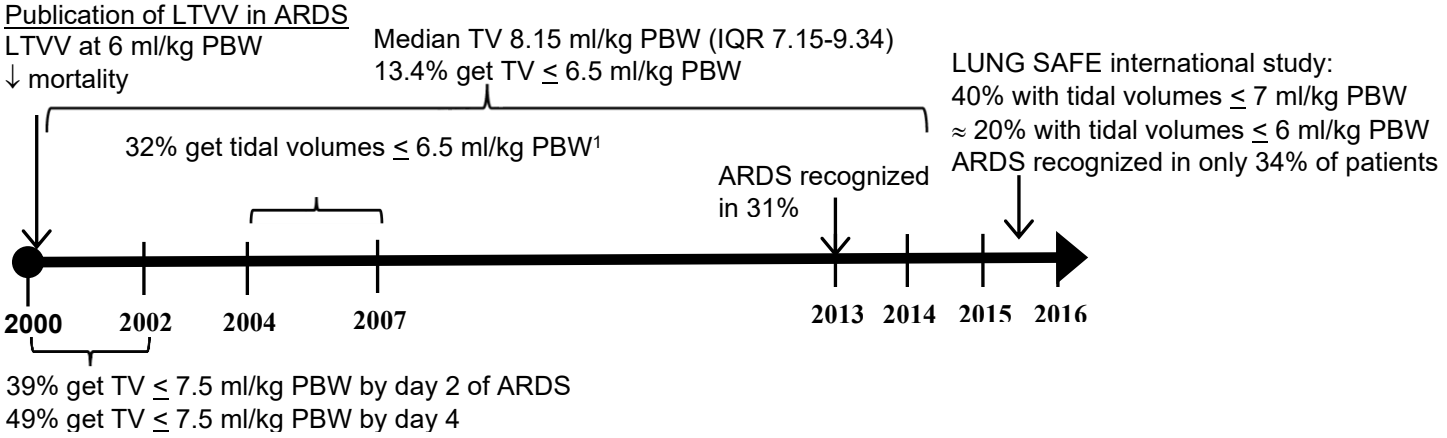
SCOPE:

Background and Context:

Acute respiratory failure (ARF) is the most common acute organ dysfunction in US hospitals, with incidence of 430 episodes/100,000 population with most (70%) requiring mechanical ventilation.[3] The most severe form of respiratory failure is Acute Respiratory Distress Syndrome (ARDS) which affects 23.4% of all ARF patients on mechanical ventilation.[4] It is a major contributor to the death of hospitalized patients with a mortality rate of 40%, prolonged hospital stays, frequent re-admissions, and high costs in the hospital.[4] Because ARDS develops after some initial injury, it is often not recognized, even as ARDS is a major contributor and driver to the mortality reported by better recognized conditions such as trauma, pneumonia, sepsis, and influenza.

While proven therapies and evidence-based systematic reviews and clinical practice guidelines exist for the management of ARDS, ARDS is consistently under-recognized and evidence-based best practices such as the use of lung protective, low tidal volume ventilation is often under-utilized in ARDS (Fig. 1). Indeed, challenges to consistent delivery of evidence-based quality care in ARDS typifies the barriers seen in many serious conditions that are commonly managed in the acute hospital setting: 1) *under-recognition* of ARDS is common; 2) as ARDS patients often present to the Emergency Department (ED) and then progress on the hospital floor before being transferred to the intensive care unit (ICU), *patient care is fractionated* among the multiple types of clinicians (physicians, nurses, respiratory therapists) with differing expertise residing in different areas of the hospital (ED, hospital floor, ICU); 3) because ARDS develops acutely and co-exists with other serious conditions like trauma or sepsis, clinical decision-making in ARDS often defaults to the automated, pattern-

Figure 1: Under-recognition of and under-utilization of low tidal volume ventilation (LTVV) in acute respiratory distress syndrome (ARDS) since the 2000 publication of benefit to LTVV.[2]



driven S1 cognitive process which is particularly *prone to unconscious biases and errors*;[5-7] 4) with over 1,000 data points per day generated for critically ill patients, clinicians caring for ARDS patients are prone to *cognitive overload leading to errors and delays in care*.[8]

To promote the consistent and timely implementation of evidence-based practices for patients with ARDS requires overcoming the barrier of under-recognition of ARDS wherever and whenever the patient may present and the barrier of under-utilization of evidence-based practices for ARDS in different clinical settings in the hospital.

Settings:

ARDS is an acute critical illness that present in hospitalized patients. This study was set up at the 3 hospitals in the Montefiore Healthcare System, a safety-net medical system serving the vulnerable and racially and ethnically diverse population of the Bronx. The 3 hospitals (Moses Montefiore, Weiler Hospital, and Wakefield Hospital) include academic quaternary and community-based urban hospitals.

Participants:

Clinical data will be extracted from all hospitalized adult patients admitted to one of 3 major hospitals in the Montefiore Healthcare System.

Incidence and Prevalence:

In a large multicenter observation cohort published in 2016, ARDS was found in 10.4% (95% CI 10.0-10.7%) of all patients admitted to an Intensive Care Unit (ICU) and 23.4% (95% CI 21.7-25.2%) of all adult patients on mechanical ventilation.[4] The estimated incidence in North America was 0.46 cases/ICU bed.

The incidence and prevalence changed with the COVID-19 pandemic. The COVID-19 pandemic flooded the hospitals with patients with acute hypoxemic respiratory failure from SARS-CoV 2 infection. Nearly all patients with acute respiratory failure on mechanical ventilators with COVID-19 pneumonia had ARDS in 2020 and 2021 and 93% of patients with COVID-19 requiring high flow nasal cannula met criteria for ARDS if they were to be intubated. This was especially acute in New York City, as it was the epicenter of the initial COVID-19 wave. Among all of New York City, the Bronx was among the most severely affected, where ICU beds at Montefiore had to be tripled and the number of mechanically ventilated patients with COVID-19 pneumonia were 5-10 times the number in other institutions outside of New York City.[9,10]

METHODS:

Specific Aim #1: To develop and validate an automated, EMR-based tool to identify patients with ARDS (ARDS Sniffer 2.0).

Study Design:

An observational retrospective and prospective cohort study of hospitalized adult patients at Montefiore Healthcare Center will be the design for Specific Aim #1 on the development and validation of the machine learning algorithm to detect ARDS or mortality in the hospital. We aimed to train a deep learning model using Long Short Term Memory (LSTM) framework and Active Learning method using historic dataset from a mechanically ventilated (MV) non-COVID cohort to identify patients with higher risk of ARDS or in-hospital mortality. We validated the model on non-COVID cohort with MV, COVID+ cohort (with and without MV), and the subgroup of COVID+ patients on MV.

Non-COVID Cohort 1 (n = 3278) was constructed in the period between January 1, 2017 to August 31, 2018. We included patients who are adults with age greater than 18 and were mechanically ventilated in the ICU, and with available arterial blood gas and ventilator settings. Each patient chart was reviewed to ascertain ARDS. In 2020, our hospital experienced an unprecedented surge in COVID-19 hospital admissions, and many required mechanical ventilation. At that point, it became important to understand how ARDS Sniffer 2.0 performed among patients with COVID-19. Therefore, we developed a separate validation cohort of

hospitalized adult patients with and without mechanical ventilation with a positive SARS-Cov-2 transcription-mediated amplification (TMA) assay from March 1, 2020 to April 17, 2020 in the COVID Cohort (n= 5672).

Ground truth labeling: ARDS gold standard identification

We defined ARDS using the Berlin criteria: hypoxemia defined as PaO2 to FiO2 Ratio (PFR) less than equal to 300 with positive pressure ventilation at least 5cmH_20, bilateral infiltrates on chest radiographs, presence of ARDS risk factors and not solely due to heart failure. For each PFR $\leq$ 300, reviewers determined if there was corresponding chest imaging supporting the presence of bilateral infiltrates as determined by physicians after standardized training session to purposely identify ARDS based on chest x-ray as per Berlin criteria.[11] Risk factors for ARDS (sepsis, shock, pancreatitis, aspiration, pneumonia, drug overdose, and trauma/burn) were determined from chart review. We use the first date and time of PFR $\leq$ 300 with confirmed bilateral infiltrates on radiograph within a 24 hour period as the time of ARDS presentation.

Active Learning

To increase the size of the dataset, we used the "active learning" technique to provide additional adult mechanically ventilated patients[12] for training. Active learning is commonly used when labeling data is time-consuming and expensive. The goal of active learning is to improve the model while keeping the size of the training dataset to a minimum by actively sampling the most valuable instances for training. We used active learning to develop a training set from patients who were admitted to the hospital from July 2016 to December 2016 and September 2018 to December 2019 (AL-Cohort). A preliminary recurrent neural network was developed using Long Short-Term Memory (LSTM) model and trained with the original non-COVID cohort. Next, we applied the preliminary model on all the mechanically ventilated patients in AL-Cohort and used pool-based sampling and uncertainty techniques to identify records from AL-Cohort to be reviewed and labeled by clinicians. The uncertainty technique includes patients whose scores are very close to the cutoff, which means the model is least confident about them. We chose a cutoff of 0.80 and selected all records with a score between 0.75 to 0.85. MV Non-COVID Cohort 2 consisting of 627 patients was derived from the active learning process using patients with acute respiratory failure admitted to the ICU from July 2016 to December 2016 and July 2018 to December 2019. This MV Non-COVID Cohort 2 were the top 1% of high score (n = 39 (6.2%)), lowest 1% (n = 35 (5.6)), and medium scored group (n = 552 (88.2%)) assigned by the preliminary model trained on MV Non-COVID Cohort 1. MV Non-COVID Cohort 2 was enriched by active learning to include 319 (50.9%) with ARDS and 246 (39.4%) who died within the hospitalization. We combined both MV Non-COVID Cohort 1 and 2 to create the MV Non-COVID Cohort (N = 3905, ARDS n = 1646 (42.2%), in-hospital mortality n =1033 (26.5%)).

Data Sources/Collection:

Clinical data was collected through automated abstraction of EHR data. All sites use EPIC as their EHR, and all clinical patient level data and process of care data are abstracted from the EHR for analysis. Raw EHR data for each admission was abstracted from admission to the discharge and were sampled and validated prior to input into the model for derivation and validation. The EHR data included demographic information (age and gender), vital signs, laboratory test results, administered medications, and so on.

Intervention:

None.

Measures:

To determine the performance of ARDS Sniffer 2.0, sensitivity, specificity, positive predictive value, negative predictive value, numbers needed to evaluate, FI score were calculated.

Limitations:

The major limitation was the change in the clinical conditions of the patient population being studied in 2020. Originally, ARDS Sniffer 2.0 was designed to help with the under-recognition of ARDS which has been consistently underreported. However, the COVID-19 pandemic resulted in an unprecedented surge of hospitalized patients with COVID-19 pneumonia, almost all of whom meet criteria for ARDS when they progress to mechanical ventilation. Consequently, we validated the model on separate cohorts of patients with COVID-19.

Specific Aim #2: To develop an evidence-based, context-appropriate, Electronic Clinical decision support system in ARDS (ECARDS) for the management of ARDS and an ARDS Dashboard for audit and feedback.

Study Design:

This aim consisted of a systematic literature review and surveys, interviews and focus groups with critical care and emergency medicine physicians.

For the systematic review, we conducted a review of reviews, focusing on pre-appraised guidelines, meta-analyses, and systematic reviews. Clinician co-authors identified an initial set of reports linking EBPs to mortality and/or duration of MV. We also searched Scopus, CINAHL, and PubMed from January 2016 to January 2019 for additional reports that provided recommendations that have not yet been incorporated into current guidelines.

Next, we surveyed the research team and clinicians with the Guideline Implementability Appraisal (GLIA) tool determine which of the EBPs identified from the systematic review was considered appropriate for implementation in an electronic modality. Then we developed metrics that would quantify the compliance to each of the EBPs and validated them against outcomes such as mortality, duration of mechanical ventilation and ventilator free days. Metrics that were feasible to calculate from commonly collected EHR data and that correlated significantly with clinical outcomes were then selected as EHR-based Performance Measures (EPMs) that will be used to measure and track compliance to EBPs in ARDS.

To understand the clinicians' thought process in managing patients with acute respiratory failure and ARDS, and their views of the benefits and barriers to clinical decision support in ARF and ARDS, we conducted think-aloud studies and semi-structured interviews. The first part of the interview was designed to understand the data elements physicians required to make diagnostic and management decisions for patients with ARF and ARDS as they verbalized their thought process when deciding how to manage 4 typical patients with ARDS. Data elements that were mentioned including how they would use it were recorded and counted. The second part focused on the clinician's attitudes towards EBPs in ARDS management. We asked for the barriers and facilitators for implementing each component of management. Lastly, the interviewees discussed their interaction with the current electronic health record (EHR) system and the use of clinical decision support system (CDSS).

Each interview was recorded and transcribed and uploaded to NVivo12 qualitative data analysis software (QSR International Pty Ltd. Version 12 2018). This was thematically coded. We also mapped the use of evidence based practices with theoretical domain framework (TDF) to understand the barriers and facilitators of evidence based practices in ARDS management. The interactions with EHR and CDSS were coded for positive or negative sentiment, and suggestions for improvement.

Guided by the input from the interviews, ARDS Sniffer 2.0 and EPMs developed above were incorporated into an electronic dashboard and ICU Reporter tool (ECARDS). This tool was created in a simulated sandbox for the research team to evaluate.

Data Sources/Collection:

The data source includes published reviews, clinical practice guidelines, meta-analyses, and systematic reviews on ARF and ARDS. For the views of clinicians, data source included the surveys and interviews with clinicians.

Intervention: None

Measures: In qualitative interviews, there are no pre-defined measures as we are interested in the views of the clinicians.

Limitations:

The major limitations to the methods are the onset of the COVID-19 pandemic in 2020, and subsequent waves from the Delta and Omicron variants in 2021 and 2022, which made ARDS much more common with greater utilization of low tidal volume and proning.

Specific Aim #3: To evaluate the effectiveness of the ARDS Sniffer 2.0 and ECARDS in a real world clinical setting.

Study Design:

The design proposed for this study is a stepped wedge clustered randomized controlled trial.

Intervention:

The pre-intervention control condition will be usual care: that is, clinicians practice as usual without clinician notification of ARDS status and without prompting by ECARDS. ARDS Sniffer 2.0 will run in the background to identify patients with Likely and Very Likely ARDS for data collection. However, clinicians will be blinded to ARDS status and ECARDS recommendations.

The intervention for this study will consist of 3 parts: 1) education of clinicians in ED, respiratory therapy, and intensive care unit on ECARDS and the clinical practice guidelines in ARDS; 2) clinicians for patients who trigger the electronic ARDS screen as Likely or Very Likely ARDS will be notified; 3) ECARDS will be delivered to the clinicians taking care of patients with Likely or Very Likely ARDS.

Measures:

The primary measures include the use of lung protective ventilation (tidal volume 4-8 cc/kg PBW and $\leq$ 6.5 cc/kg PBW) compliance with daily spontaneous awake trials, spontaneous breathing trials, and avoidance of oversedation into coma. Other outcome measures include hospital mortality, ICU and hospital length of stay, and 28-day ventilator free days.

Limitations:

The major limitations to Aim #3 are the onset of the COVID-19 pandemic in 2020 and subsequent waves from the Delta and Omicron variants in 2021 and 2022 which changed the landscape of ARDS management and strained hospital resources to develop the machine learning algorithms and decision support tool in real time for the trial. While ARDS Sniffer 2.0 and ECARDS were developed and validated, the generation of provider-directed real time alerts was delayed and incorporation into the clinical environment for testing was postponed. Resources for IT development had been re-directed to clinical management to respond to COVID-19 pandemic and then to the recovery of clinical operations after each wave of the pandemic. In addition, administration was reluctant to build alerts given the changing prevalence of ARDS depending on the COVID-19 surge and physician increased recognition of ARDS because of the pandemic. They have asked for updated data on prevalence of ARDS when not in the midst of a COVID-19 surge, clinician recognition of ARDS after the pandemic, more current data on compliance to evidence-based practices that are in ECARDS to see if the trial is still necessary.

RESULTS:

Principal Findings and Outcomes

Specific Aim #1: To develop and validate an automated, EMR-based tool to identify patients with ARDS or high likelihood of mortality.

In developing the ARDS Sniffer 2.0, we had included in the model radiological findings from radiology reports of the lung using natural language processing. However, the inclusion of the chest radiograph report did not significantly improve the performance of the model, but it did delay the timeliness of the notification (i.e.: the model with radiological report alerted later than the model without radiologic data). As a result, we used the model without chest radiograph data. This LSTM model for identification of risk for ARDS or in-hospital mortality was tested on 3 populations: a mechanically ventilated pre-COVID population, a mechanically ventilated and non-ventilated COVID population and the sub-group of COVID patients who were mechanically ventilated. The characteristics of the cohorts are described in Table 1:

Table 1: Cohorts characteristics

		Training	Validation		
Variables	**MV Non-COVID cohort**	**MV Non-COVID (Training) Cohort**	**Non-COVID (Validation) Cohort**	**COVID Cohort**	**MV COVID sub-cohort**
n	3905	3124	781	5672	803
Age, yr, mean +/-SD	65.0 ± 14.7	65.0 ± 14.8	65.3 ± 14.4	60.80 ± 17.2	62.1 ± 13.9
Gender					
Male, n (%)	1741 (44.6)	1437 (46)	328 (42)	2665 (47)	319 (40)
Female, n (%)	2164 (55.4)	1686 (54)	452 (58)	3006 (53)	484 (60)
Race or ethnicity					
White, n (%)	1015 (26)	749 (24)	249 (32)	623 (11)	177 (22)
Black, n (%)	1718 (44)	1405 (45)	320 (41)	2495 (44)	345 (43)
Other, n(%)	1171 (30)	968 (31)	210 (27)	2552 (45)	281 (35)
ARDS Determination					
PaO2/FiO2 Ratio < = 300, n (%)	3211 (82.2)	2579 (82.6)	632 (80.9)	617 (10.9)	617 (77)
CXR interpretation					
Yes (consistent with ARDS), n (%)	1333 (34.1)	35.4 (35.4)	260 (33.3)	565 (10)	565 (82)
Indeterminant, n (%)	313 (8.0)	7.1 (7.1)	60 (7.7)	18 (.3)	18 (2.2)
No (not consistent with ARDS), n (%)	2259 (57.8)	57.6 (57.6)	461 (59)	34 (.6)	34 (4.2)
Risk Factors					
Aspiration, n (%)	407 (10.4)	10.3 (10.3)	86 (11)		
Shock, n (%)	1520 (38.9)	39.2 (39.2)	299 (38.3)		
Pneumonia, n (%)	1530 (39.2)	39.8 (39.8)	288 (36.9)	5672 (100)	803 (100)
Sepsis, n (%)	1885 (48.3)	48.8 (48.8)	362 (46.4)		
Pancreatitis, n (%)	42 (1.1)	1.1 (1.1)	9 (1.2)		
Burn, n (%)	3 (0.1)	3 (0.1)	0 (0)		
Overdose, n (%)	98 (2.5)	2.5 (2.5)	21 (2.7)		
Transfusion, n (%)	1191 (30.5)	30.7 (30.7)	232 (29.7)		
Congestive Heart Failure, n (%)	914 (23.4)	23.6 (23.6)	178 (22.8)		
Presence of at least 1 risk factor, n (%)	2739 (70.1)	70.6 (70.6)	362 (46.4)	5672 (100)	803 (100)
Clinical Outcomes					
Mechanically ventilated, n (%)	3905	3124	781	803 (14.2)	803
ARDS, n (%)	1646 (42.2)	1326 (42.4)	320 (41.0)	583 (10.3)	583 (72.6)
In-hospital Mortality, n (%)	1033 (26.5)	848 (27.1)	185 (23.7)	907 (16.0)	418 (52.1)
ARDS or In-hospital Mortality, n (%)	2044 (52.3)	1655 (53.0)	389 (49.8)	1235 (21.9)	746 (92.9)

The LSTM model performed well in each test cohort with an area under the curve (AUC) and F1 score of 0.78 and 0.75 for the MV Non-COVID cohort, 0.83 and 0.61 for COVID patients and 0.70 and 0.93 for the subgroup of MV COVID patients. The sensitivity for identifying ARDS was 86% in the MV non-COVID patients with a positive predictive value (PPV) of 66% and numbers of alerts needed to evaluate to find one case of ARDS or mortality being 1.52 (Table 2). This value suggests that, on average, for every 3 alerts from the ARDS Sniffer 2.0, 2 alerts will be confirmed to be ARDS or die before ARDS could be confirmed and this would capture the majority (86%) of the patients with such an outcome. Given the COVID-19 pandemic, we also tested the model in mechanically ventilated patients with COVID-19. The model performed equally well with a sensitivity of 92%, but because almost all patients with COVID-19 had ARDS, 73% of the patients will trigger the alert and nearly every alert will be confirmed to be ARDS (PPV is 94% and Number of alerts needed to be evaluated to find one confirmed ARDS patient is 1.06). Of note, although ARDS Sniffer 2.0 still performs very well in COVID-19,

Table 2: Performance of ARDS Sniffer 2.0 in different cohorts

TREAT-ECARDS model diagnostics	MV Non-COVID Cohort	COVID Cohort	MV COVID sub-cohort
Sensitivity	0.86	0.7	0.92
Specificity	0.57	0.84	0.23
Positive Predictive value	0.66	0.55	0.94
Negative Predictive value	0.8	0.91	0.17
Receiver operating curve	0.78	0.83	0.7
F1 Score	0.75	0.61	0.93
Number needed to evaluate	1.52	1.82	1.06

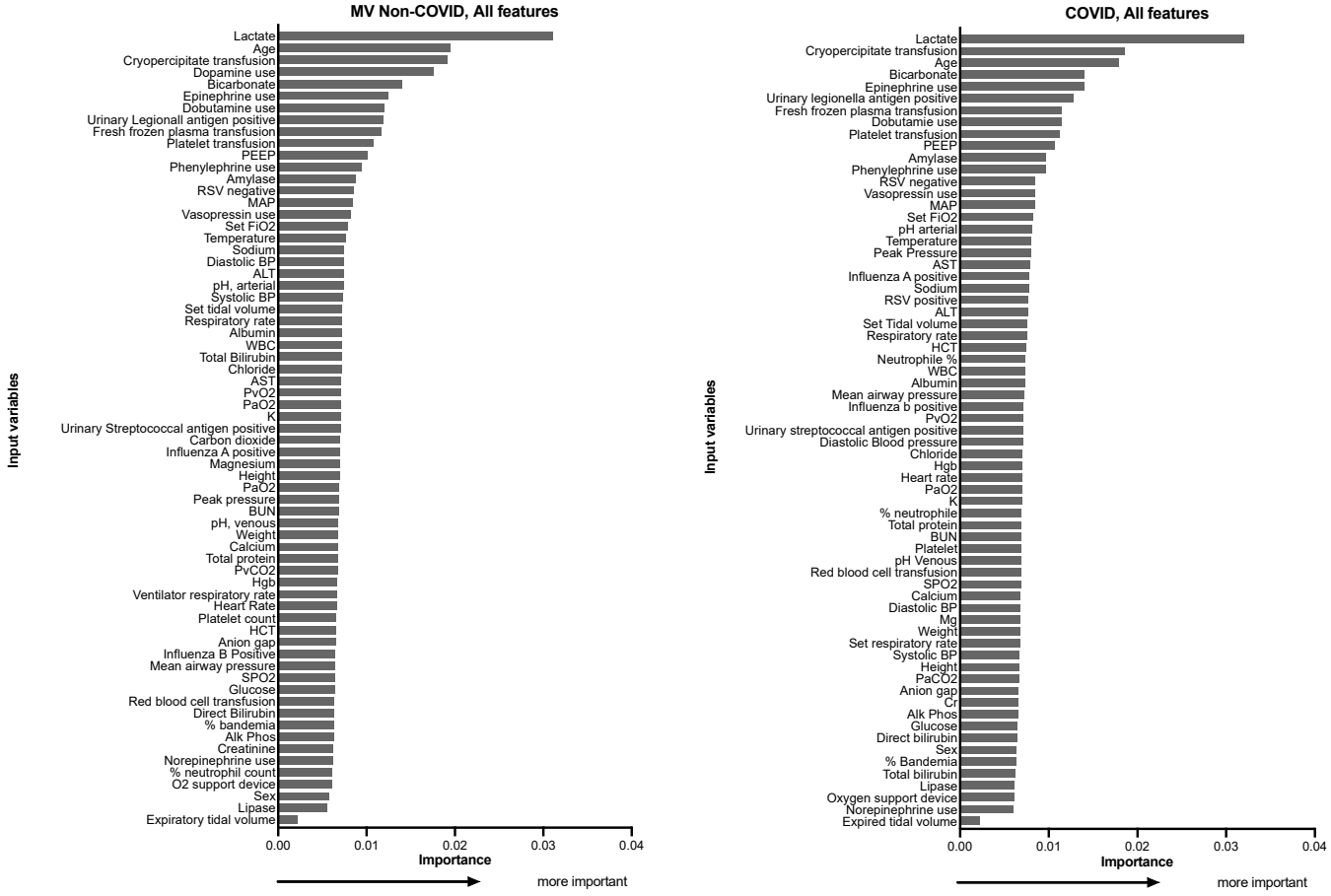
Table 3: Timeliness of ARDS Sniffer 2.0 to identify or predict ARDS or mortality

	n	Correctly identifies, n (%)	Time from Intubation, median (IQR), hours	Before intubation, n (%)	After intubation, n (%)	Time from ARDS label, median (IQR), hours	Before ARDS, n (%)	After ARDS, n(%)	Time from death median (IQR), hours
MV Non-COVID Cohort									
ARDS	204	166 (81.4)	0 (-12.8, 26.0)	87 (52.4)	79 (47.6)	0 (-43.8, 12.0)	115 (69.3)	51 (30.7)	
Death	69	60 (87)							-225.5 (-461.3, -101.3)
ARDS and Death	116	108 (93.1)	-1 (-38.8, 9.3)	68 (63.0)	40 (37.0)	-20 (-115.5, 0.3)	81 (75.0)	27 (25.0)	-314 (-588.5, -127.8)
ARDS or death	389	274 (70.4)	-1 (-17.8, 15.0)	155 (56.6)	119 (43.4)	-10.0 (-75.5, 4.0)	196 (71.5)	78 (28.5)	-225.5 (-461.3, -101.3)
No ARDS or death	392	223 (56.9)							
COVID Cohort									
ARDS	328	318 (97)	3 (-8.8, 11.0)	136 (42.8)	182 (57.2)	0 (-16.0, 9.0)	141 (44.3)	128 (40.3)	
Death	652	308 (47.2)							-58 (-112, -20)
ARDS and Death	255	237 (92.9)	4 (-1, 18)	86 (36.3)	156 (65.8)	0 (-12, 10)	125 (52.7)	112 (47.3)	- 112 (-211.3, -52)
ARDS or death	1235	555 (44.9)	3 (-3.5, 13.0)	222 (40.0)	333 (60.0)	0 (-14.0, 10.0)	266 (47.9)	240 (43.2)	-58 (-112, -20)
No ARDS or death	4437	3724 (83.9)							
MV COVID Sub-Cohort									
ARDS	328	318 (97)	3 (-8.8, 11.0)	136 (42.8)	182 (57.2)	0 (-16.0, 9.0)	141 (44.3)	128 (40.3)	
Death	163	128 (78.5)							-37 (-87, -11)
ARDS and Death	255	237 (92.9)	4 (-1, 18)	86 (36.3)	156 (65.8)	0 (-12, 10)	125 (52.7)	112 (47.3)	- 112 (-211.3, -52)
ARDS or death	746	555 (74.4)	3 (-3.5, 13.0)	222 (40.0)	333 (60.0)	0 (-14.0, 10.0)	266 (47.9)	240 (43.2)	-37 (-87, -11)
No ARDS or Death	57	13 (22.8)							

the high prevalence of ARDS makes even a well-performing model unnecessary for detection. Clinicians are already assuming that most patients will have it. The model was originally designed to identify patients on mechanical ventilation with ARDS, but ARDS Sniffer 2.0 was actually able to identify more than half of the MV non-COVID patients (52.4%) as being at high risk for ARDS or mortality before intubation and before meeting criteria for ARDS. The model identified patients at risk for ARDS or death at a median of 10 hours and an interquartile range (IQR) of -75 to 4 hours prior to ARDS and 225 hours or 9 days (IQR, -461 to 101 hours) prior to death in the hospital (Table 3). In the COVID-19 Cohort, the model was less timely. It was able to identify the patient as likely to have ARDS or in-hospital mortality 3 hours after intubation (IQR, -3.5 to 13.0 hours) at the time of patient fulfilling PaO2/FiO2 criteria for ARDS (median time 0 hours from ARDS time (IQR, -14.0 to 10.0) and median of 37 hours (IQR, 87 to 11 hours) before death.

The features that were important in the algorithm in determining risk are similar between both the COVID and non-COVID populations (Figure 2). The most important features in discriminating patients with and without ARDS or high mortality are indicators of severity of illness (vasopressor use, transfusion needs, acidosis) and oxygen requirements (blood gas and FiO2).

Figure 2: Important features in the model in identifying ARDS or in-hospital mortality



Specific Aim #2: To develop an evidence-based, context-appropriate, Electronic Clinical decision support system in ARDS (ECARDS) for the management of ARDS.

Identification of Evidence-Based Practices (EBPs) in ARDS and Acute Respiratory Failure to Implement in ECARDS

To develop an evidence-based clinical decision support tool, we first did a systematic review of all interventions found to improve mortality or decrease duration of mechanical ventilation in patients with ARDS or ARF. We did this for 3 phases of ARDS and ARF: Phase 1 involved initiation of mechanical ventilation,

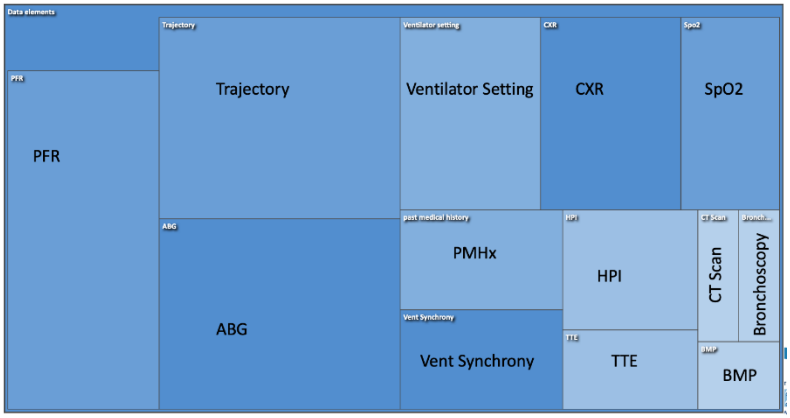
Phase 2 involved prevention of complications and lung injury during mechanical ventilation and Phase 3 which involves extubation and discontinuation of mechanical ventilation. We identified a total of 20 EBPs. In Phase 1 (initiation of IMV and intubation), 6 EBPs were identified which includes conservative oxygen therapy, avoidance of high driving pressure, lung protective ventilation, neuromuscular blockades, positive-end expiratory pressure, and prone positioning. We identified 10 EBPs as Phase 2 (prevention of complications during IMV). These include analgesia first approach to sedation and pain management; conservative fluid management; delirium assessment, prevention, and management; early mobility protocols; glucocorticoid treatment; high-frequency oscillatory ventilation; sedation protocols; sleep management; spontaneous awakening trials; and spontaneous breathing trials. There are 4 EBPs in Phase 3 (extubation and discontinuation of IMV): cuff leak tests, extubation to high flow or non-invasive mechanical ventilation, and use of a ventilator liberation protocol.

During the course of the project, there were several publications of impactful trials that reduced the level of evidence supporting EBPs such as neuromuscular blockade[13], high PEEP[14], conservative oxygen therapy[15], extubation to high-flow or non-invasive mechanical ventilation[16]. As a result, these EBPs were dropped from consideration for implementation.

Think-Aloud Studies and Semi-Qualitative Interviews with Clinicians to Inform the Development of ECARDS

We conducted 8 interviews with attending physicians from the Division of Critical Care Medicine at Montefiore Medical Center. The attending physicians interviewed had a range of clinical experience with years in practice ranging from 1 to 20 years (median of 9 years). Two physicians practiced in the Medical ICU, 1 in the Surgical ICU, 2 on the Critical Care Consult Service, 1 in the Neurology ICU, and 2 in the Cardiothoracic ICU. Most were internal medicine trained, except for one who had completed a neurology residency. All 8 had completed training in critical care fellowship. 2 had additional training in pulmonary, 1 in nephrology, 1 in infectious disease, 1 in neurology, and 1 in palliative care. All attending physicians consented to interviews.

Figure 3: Data elements used in ARF and ARDS by Critical Care attending physicians at Montefiore Medical Center. The size of the box reflects the number of participants who requested the data element and the shade of the box reflects number of times the data is mentioned by participants (darker the shade the more times the data is mentioned).



We first asked participants about data that they most commonly need to make decisions about whether a patient has ARDS and how they should be managed. The most commonly requested data element was PaO2 to FiO2 ratio (PFR), follow by arterial blood gas (ABG) and the trajectory of the patient. Ventilator settings and synchrony are also important to the interviewees (Figure 3). Interestingly, lung imaging by chest radiograghs (CXR) or by CT scan were not commonly asked for, even as it is part of the formal criteria for ARDS.

We then asked the participants about what, in their view, helps or hinders the implementation of EBPs about ARDS identified from the systematic review. Their responses were then mapped to Theoretical Domain Framework to better understand the potential barriers and facilitators to these EBPs in practice (Table 4). The above indicated several areas to target during implementation including training of nurses, electronic calculation of tidal volume to overcome the knowledge gap about how low tidal volume is calculated, automated abstraction height from prior medical records to enable calculation of tidal volume. Some statements about sedation also re-enforces the selection of EBP on avoiding oversedation to coma.

Table 4: ARDS management modalities and TDF domains, with examples

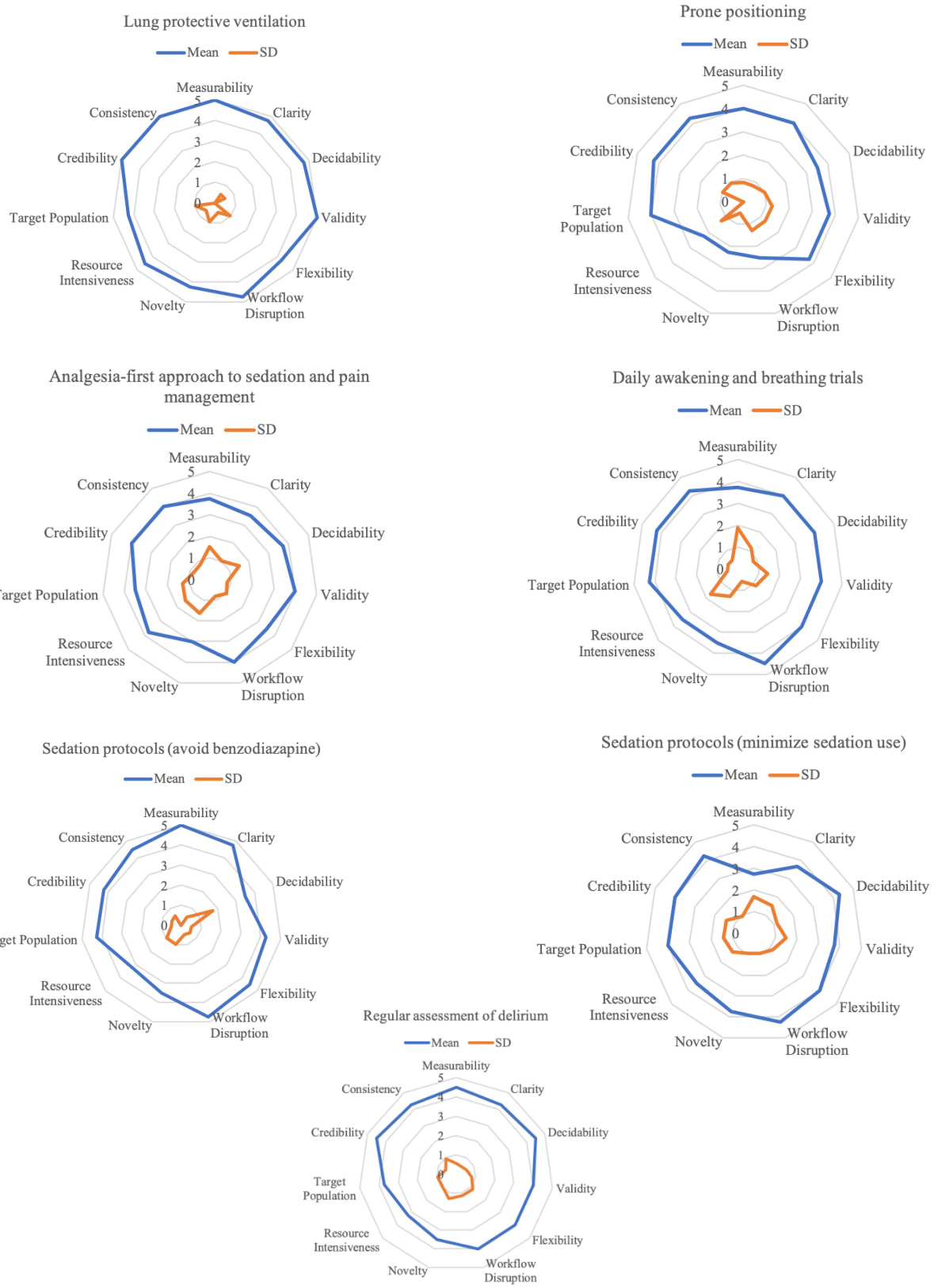
Management modalities	TDF domain	Example
Lung protective ventilation	Knowledge	"Um, I think some of it has to do with **lack of knowledge** on some caregivers' part. **Some of it can just be habitual behavior in terms of what normal tidal volume should be with somebody on a ventilator.** Sorry, can't see my hands, quote unquote normal tidal volume would be for someone on a ventilator. And I think also even when they do try to apply a low tidal volume strategy, **some people might forget that it's actually based upon a person's ideal body weight** not their actual body weight, so that could also be an issue. So, they may not be able to apply it. They may know about it but not be able to apply it properly. They may not know about it at all. Or they may just be creatures of habit I think would be the major stumbling blocks to providing low tidal volume lung protective strategy." "**Getting an accurate height**, unless you're walking around—I know that a couple of the attendings walk around with tape measures themselves... I do not have a tape measure. I probably should get one. But that would be that's probably the biggest thing is that **you're assuming that it's low tidal volume like ventilation or but it's not necessarily so if the height's way off**."
PEEP	Beliefs about capabilities	"PEEP ....Um, I think a lot of people are afraid of it, unnecessarily so.... **It's nothing to be afraid of.** You just have to understand how to use it and how to use it properly.
Sedation	Environmental context	"That's very much a nursing thing. Like **depending on who's watching the patient and who's taking care of the patient at bedside**..... Um, because it makes people happy to have like a nice, calm patient. **It makes work a little easier**. It makes your life a little easier if the patient's not bothering you or trying to—you don't have to worry about them necessarily pulling out their (tracheal tube)" "the barrier to for me for severe ARDS, again**, I mean I would say the biggest barrier is nursing.** I mean what I have seen, and this is differs slightly from campus to campus too, but what I have seen is like automatically the nursing would aim for minus 5. And I ask them, **"Why are you doing minus 5 for this patient?" "Oh, Doctor, the patient is on two pressors." But that's not the reason to keep them minus 5."**
Prone positioning	Environmental context and belief about capability	"So, there were a couple of times where we wanted to do it and they were **really short on nurses**, things like that... Having senior nurses who have done it before [helps]" "Right. I mean so I mean**, I do not have much experience with the proning**, because I mean in my previous job also we had very low threshold of taking them to ECMO. So it's only after coming here I've seen like four, five patients that I've taken care of myself who were proned. **So, proning, I am a little less comfortable with or less something that I have experience with**."
Neuromuscular blockade	Beliefs about capability	"But neuromuscular paralysis**, I have a very low threshold**. If I see PO2/FIO2 ratio has been—I mean I know the trial was 150 and less than that. But I usually my threshold is less than 100. And if I see less than 100 PO2/FIO2 ratio, I used to start them on like [0:07:57] bolus followed by the drip and keep them paralyzed for 48 hours. But I mean sometimes in once in a while I have done this, I have given them break from paralysis, I mean for few hours, and then maybe just rebolus rather than starting the whole drip again. But this is on a case by case basis. **But again, do I use only vent desynchrony for paralysis? No, I used to paralyze almost everyone with the PIO2/FIO2 less than 100. And I mean, without looking at any of that because that would give me full control of the patient**, I would be able to control peak and plateau, I would be able to come down on the FIO2 and I keep them on a high PEEP strategy and open lung strategy, so I keep coming down on FIO2."
Steroid	Environmental context	"Um, so steroids tend to be on every patient that comes into this hospital. So, whether it's for ARDS or it's for their shock state or for some other reason, pretty much everyone who has ARDS is already on steroids. So, it's not something that I've had to necessarily consciously think about putting on for ARDS, specific intent of treating ARDS. But I don't have an issue with starting it, (I mean) steroids.

Prioritization of Evidence-Based Practices to Include in ECARDS

In a survey of the research team and 42 practicing ICU clinicians from 8 health care systems from across the US, we then prioritized the EBPs based upon input from clinicians taking care of such patients and upon their perceived readiness for implementation in an electronic digital fashion using the Guideline Implementability Appraisal (GLIA) tool. This reduced the 20 EBPs identified from the systematic review to 7 EBPs determined by the research team and the survey to be important to include in the electronic clinical

decision support tool and to be amendable for electronic delivery under the GLIA tool (average rating across all domains of GLIA is ≥4 with no domains < 3) (Figure 4). Prone positioning was included, even as the rating for resource intensiveness was high and novelty was low (<3 for both) because it was deemed to be important for ARDS management by the research team and survey of clinicians. Minimizing sedation was also included,

Figure 4: Results from Guideline Implementability Appraisal Tool for Evidence-based practices in ARDS and Acute Respiratory Failure



even as it rated below 3 for measurability by the clinicians because the research team could test the measurability using EHR data in the next step.

Development of Dashboard (ECARDS) to Identify Patients at High Risk for ARDS or Mortality and to Report on the Adherence to Evidence-Based Practices in ARDS and Acute Respiratory Failure

In order to have an electronic dashboard to track compliance to EBP identified above, the research team then investigated the feasibility of calculating Electronic Health Record (EHR) based performance metrics (EPM) for each of the EBPs. We know from prior research with our collaborators that compliance to low tidal volume ventilation can be calculated in different ways and that most calculations do not correlate with mortality of mechanically ventilated patients. However, calculation of duration of exposure to high tidal volume (> 8 cc/kg Ideal body weight (IBW)) does correlate with mortality. We confirmed this finding in a different population of patients at Montefiore as part of this project. We found that even though the goal is to set low tidal volumes on the ventilator for patients with ARDS, the achievement of low tidal volume did not correlate with mortality and duration of mechanical ventilation. Rather, it was the duration of exposure to high tidal volume that correlated best to outcome. Exposure to tidal volumes greater than 8 cc/kg IBW for more than 12 hours was associated with higher mortality, longer ICU and hospital length of stay, more days on the mechanical ventilator and less days alive and free of mechanical ventilation (Table 5).

Table 5: Association Between the Electronic Health Record-Based Performance Measures for Exposure to High Tidal Volume ≥ 8 cc/kg IBW for more than 12 hours and Clinical Outcomes in ARDS

Outcome	Effect
Hospital Mortality	OR= 1.12 95% CI 1.01-1.25
Hospital Length of Stay	+3.90 Days difference
ICU Length of Stay	+2.76 Days difference
Ventilator Days	+1.86 Days difference
28 day Ventilator-Free Days	0.72 95% CI 0.68-0.76

Consequently, we investigated different methods for measuring compliance to EBPs identified from the prior steps to determine the feasibility of calculating EPMs for each of the identified EBPs above.

Table 6: Evidence-based practices (EBPs) in ARDS and acute respiratory failure and proposed EHR-based measures (EBMs) for measuring and tracking compliance to practices

Evidence-Based Practice (EBP)	EHR-Based Performance Measure (EPM)	Rationale
Lung protective ventilation	• Percentage of hours of mechanical ventilation with tidal volume > 8 (or 6.5) cc/kg IBW • More than 12 hours with TV > 8 (or 6.5) cc/kg IBW • More than 24 hours with TV > 8 (or 6.5) cc/kg IBW	Goal is to minimize time that an ARDS patient is NOT receiving lung protective ventilation (ie: receiving high tidal volumes). In collaboration with our Michigan colleagues (see below), we showed duration of exposure to "high" tidal volume correlated with mortality and showed greater variability across ICUs than other measures of low tidal volume (TV) use
Spontaneous awake trials	• Percentage of eligible MV days patients had spontaneous awake trial	Goal is to provide metrics for clinicians to assess how well they are able to reach the evidence based recommendation of minimizing sedation to allow patients to be awake and comfortable
Spontaneous breathing trials	• Percentage of eligible MV days patients had spontaneous breathing trial	Goal is to provide metrics for clinicians to assess whether they assess for extubation as soon as possible and on all potentially eligible days
Coordinated spontaneous awake and breathing trials when ready	• Percentage of eligible MV days patients had both spontaneous awake and breathing trial	Goal is to provide metrics to promote SAT and SBT on as many eligible days as possible
Avoid use of benzodiazepine for sedation	• Percentage of eligible hours on MV receiving any continuous benzodiazepine for sedation	Goal is to minimize time receiving benzodiazepine
Minimize coma during sedation	• Percentage of eligible hours on MV spent in a coma (RASS -5)	Goal is to minimize time on MV spent in coma and still getting continuous sedation

We then correlated the EPMs with clinical outcomes and demonstrated that greater compliance with EBP as measured by the EPMs was associated with lower mortality (Figure 5), shorter ICU and hospital length of stay, and higher ventilator free-days (Figure 6) in a dose dependent manner. We then planned to incorporate these EPMs into the ECARDS dashboard. Ultimately, assessment for delirium and proning was dropped as one of the EBPs because of inability to accurately track this in the medical records. The nursing documentation of CAM-ICU for delirium was inconsistent across the different ICUs and prone positioning was not documented, except as free text in progress notes which are not readily abstractable from the EHR. The final list of EBPs with associated EPM for ECARDS are detailed in Table 6.

Figure 5: Adjusted association of different compliance to EBP metrics and in-hospital mortality. We adjusted for age, sex, race, APACHE III physiology score, ICU types, and each ICU as random effect.

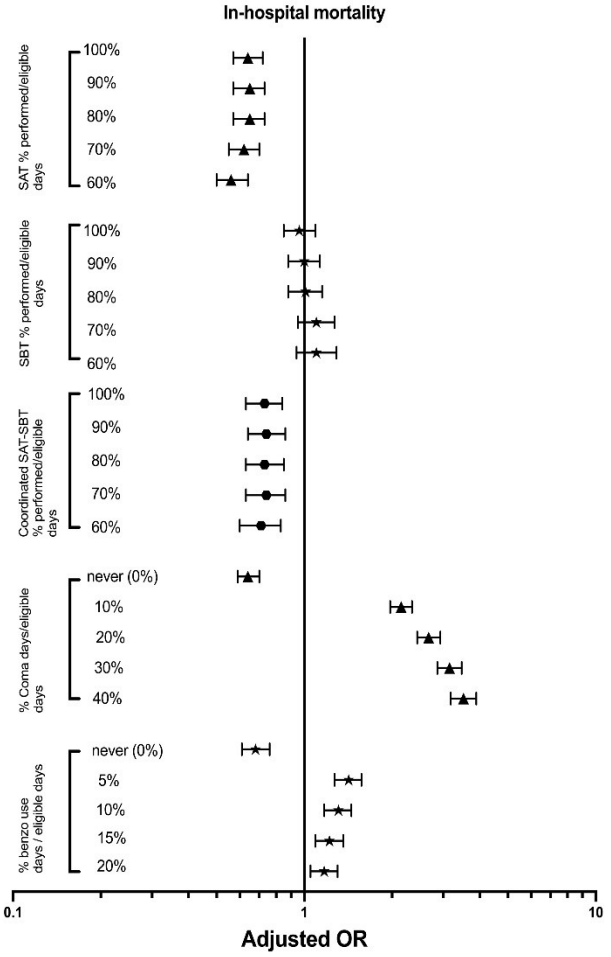
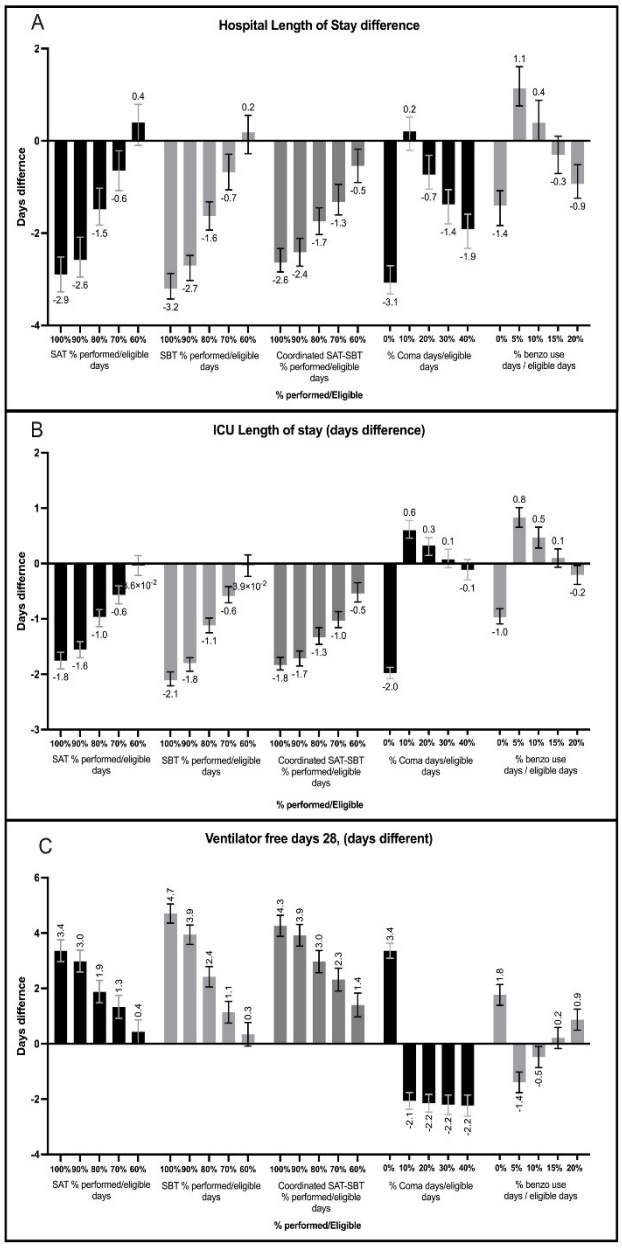


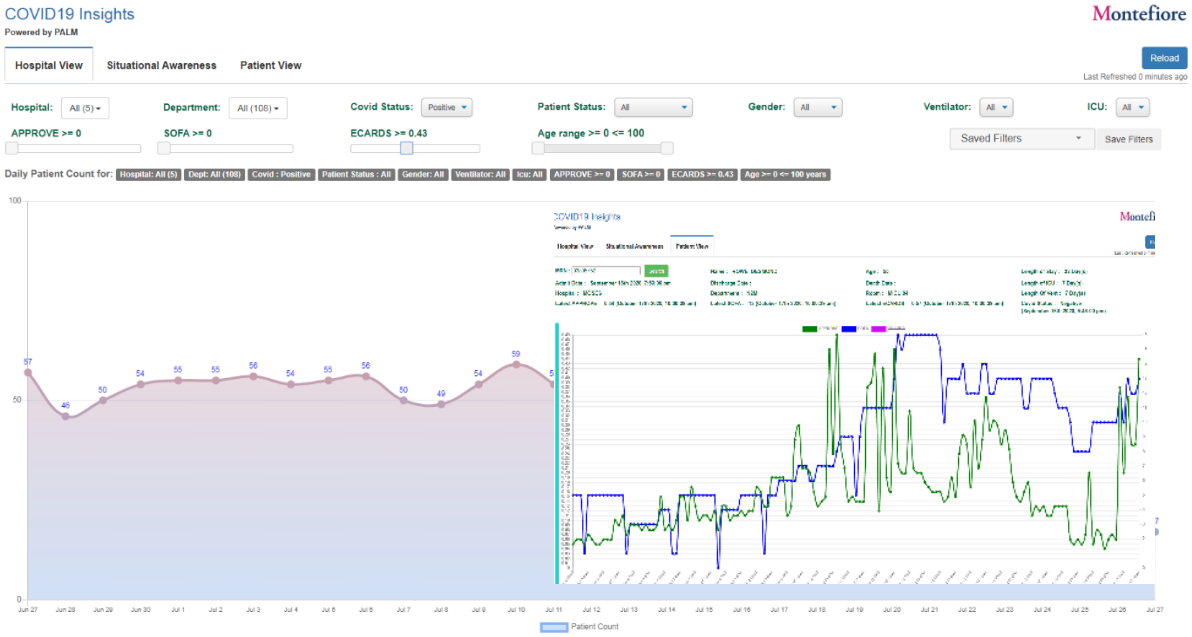
Figure 6: Adjusted days difference in hospital and ICU length of stay and ventilator free days at 28 days. Adjusted for age, sex, race, APACHE III physiology score, ICU types, and each ICU as random effect



In building ECARDS, we first developed a dashboard to allow physicians to see and identify those patients with or at high risk for ARDS or death. The ARDS Sniffer 2.0 was automated to analyze the EHR data every two hours from all patients hospitalized in the 3 hospitals of Montefiore Medical Center. In addition to the ARDS Sniffer, we also calculated the Sequential Organ Failure Assessment (SOFA) score and the previously developed APPROVE (Accurate Prediction of PROnged VEntilation) score for every patient in the hospital every 2 hours. The results of these scores were then displayed in an electronic dashboard for real time situation awareness. The dashboard exists in a simulated “sandbox” environment that was visible only to the research team. Because this occurred during the COVID-19 pandemic, we also incorporated the ability to filter

the data by COVID-19 status, location, mechanical ventilation status, and by threshold of ARDS Sniffer, SOFA or APPROVE scores. On the hospital view (Figure 7), the user can filter the report by gender, COVID status,

Figure 7: Screen shot of the ECARDS Dashboard that graphically display the number of patients that meet the filter criteria set by the user (hospital, department, COVID-19 status, gender, mechanical ventilation, location (ICU or not) and by threshold of APPROVE, SOFA, or ARDS Sniffer 2.0 ECARDS score) on each day. Clicking on a particular day will give a list of all patients who meet those criteria and clicking on a patient will display the APPROVE, SOFA, or ARDS Sniffer 2.0 ECARDS score for that patient over time



mechanical ventilation and threshold of APPROVE, SOFA and ARDS Sniffer score to give the number of patients who meet all of the filter criteria. If the user clicks the number of patients who meet the filter criteria on a particular day, a list of patients who meet those criteria appears. Clicking on any patient will bring the user to the Patient View, which graphs out the various scores during the entire admission up to this point. Given the results of the Think-Aloud study with clinicians who indicated that the trajectory of the patient's course is important in their clinical decision making in ARDS and acute respiratory failure, the dashboard was designed to show the change over time in organ failure, likelihood for ARDS (by the ARDS Sniffer 2.0) and likelihood for respiratory failure or mortality (APPROVE).

As part of ECARDS, we also designed an ICU Reporter to graphically display ICU statistics such as mortality, re-admission, length of stay and duration of mechanical ventilation among survivors for each ICU at Montefiore (Figure 8). Incorporated into this dashboard are EPMs for EBP such as spontaneous awakening trials, breathing trials, and time spent in coma while on sedation. Tidal volume and proning are not yet incorporated into this dashboard, as it is more technically difficult to link this report to the ARDS Sniffer and validation from the clinician on ARDS status given the desire by clinicians to have this measured only among those with likely or confirmed ARDS. The ICU Reporter is meant to be used by ICU directors and nurse managers to get a regular monthly report of compliance to EBPs in their ICUs in order to empower feedback and change and track progress.

Both the ECARDS Dashboard and the ICU Reporter exist in a separate server based with the research team. The hospital IT department has not allowed for its integration into the hospital EHR system just yet. While the research team can access ECARDS via a separate secure link to the research server, clinical providers cannot access these tools through the EHR system.

Figure 8: ECARDS ICU Reporter on outcomes and EHR-Based Performance Measures

Specific Aim #3: To evaluate the effectiveness of the ARDS Sniffer 2.0 and ECARDS in a real world clinical setting.

The COVID-19 pandemic completely changed the landscape of care for patients with acute respiratory failure in the hospital. The pandemic prevented us from implementing ECARDS into the clinical setting for a clinical trial for a number of different reasons. Firstly, the hospital system, including the informatics department, was prioritizing clinical response and all research efforts ceased. Although the research activity and development of the dashboard continued, the implementation of the clinical decision support tool for the clinicians to prompt compliance to EBP could not be implemented without access and support of the hospital IT infrastructure. Secondly, the COVID-19 pandemic changed the context and underlying premise for the trial. The onset of the COVID-19 pandemic in 2020 overwhelmed the hospital systems in New York City, with the Bronx and Montefiore among the most affected. The hospital was inundated with patients with COVID-19

pneumonia. Among those who were intubated for acute respiratory failure, >70% fulfilled criteria for ARDS. Prior to the pandemic, ARDS was under-recognized, but after the emergence of COVID-19, ARDS was assumed in all patients with respiratory failure and hypoxia. Even as we had developed the ECARDS dashboard to identify risk for ARDS, during the pandemic, its use was limited as nearly all patients with COVID-19 on mechanical ventilation were identified as high risk for ARDS (see above). At the same time, resource limitations in terms of respiratory therapists and nursing shortages as well as intermittent shortages of sedatives requiring use of long-acting substitutes were limiting the ability to do spontaneous awakening trials (SATs) and spontaneous breathing trials (SBTs). We examined how this might have affected the compliance to EBPs identified in Specific Aim #2 in Table 7. The avoidance of high tidal volume increased more than 3-fold to greater than 88%. The need for implementation of the ARDS Sniffer 2.0 and ECARDS to promote low tidal volume ventilation was lessened given the increased recognition and adoption of low tidal volume ventilation. However, compliance to other EBPs such as SATs and SBT worsened, but this was attributed to the staffing and drugs shortages. Prior to the clinical implementation of ECARDS to address the gaps in practice, hospital administration recognized the changed clinical landscape for acute respiratory failure after the pandemic and wanted to delay any implementation of interventions until a re-evaluation of post-pandemic clinical practice and adherence to evidence-based practices could be measured. Methodologically, this is not unreasonable since outcomes in the hospital for mechanically ventilated patients have changed over time depending on the activity of the pandemic, the slow return of non-COVID related conditions to the hospital, and the severity of illness of the COVID-19 patients being seen after the slow uptake of vaccination. Unfortunately, every time we planned for a re-evaluation; another wave of COVID-19 would occur. As a result, we could not conduct the trial as planned.

Table 7: Compliance to Evidence-Based Practices in ARDS and Acute Respiratory Failure Before and After COVID-19 Pandemic

EHR-Based Performance Measure	After COVID in 2020-2021	Pre-Pandemic in 2019
Low Tidal Volume Ventilation		
% Patients who were NOT exposed to high tidal volume (≥ 8cc/kg IBW) for more than 12 hours	471 (88.4%)	134 (22.9%)
Eligible patients, n (%)	533	584
Spontaneous Awakening Trials		
Patients with 100% performance, n (%)	167 (34)	230 (40)
Eligible patients, n (%)	487 (88)	579 (88)
Spontaneous Breathing Trials		
Patients with 100% performance, n (%)	70 (43)	279 (64)
Eligible patients, n (%)	164 (30)	436 (67)
Concomitant SAT-SBT		
Patients with 100% performance, n (%)	53 (35)	185 (48)
Eligible patients, n (%)	152 (28)	388 (59)

Specific Aim #4: To promote the dissemination of the ARDS Sniffer 2.0 and ECARDS through our partner professional organizations

The results of this project have been presented in international conferences such as the Society of Critical Care Medicine and American Thoracic Society, as well as published in peer reviewed journal (see below).

Discussion:

This project aimed to build an electronic clinical decision support tool to improve compliance to evidence-based practices in patients with ARDS and acute respiratory failure with a multi-faceted, mixed methods approach that include: 1) The development and validation of a deep learning algorithm (ARDS Sniffer 2.0) that utilizes EHR-data to identify patients with existing ARDS or with a high likelihood of progressing to ARDS or mortality; 2) Selection of EBPs to include in the tool that was informed by a systematic review of available literature and stakeholder input into its importance, feasibility and credibility; and 3) design of an ECARDS dashboard that identified, in near real time, patients with high risk of ARDS or death, and an ICU

Reporter that calculates and displays the EHR-based performance measures that correlate compliance with clinical outcomes. Such an ICU Reporter can be used to drive improvement and track progress. The design ECARDS Dashboard and ICU Reporter was done with consideration to the input from clinicians who take care of patients with ARDS.

This multi-modality strategy is important as it can reconcile the empiric data driven strategies with the user centered perspective which may or may not correlate with each other. For example, one defined criteria for ARDS is the presence of bilateral infiltrates on chest radiographs. However, in our modeling of ARDS Sniffer 2.0, the addition of radiographic reports did not substantially improve the performance of the model, but did delay the identification of ARDS in patients. What was important in the model for discrimination was indicators of how sick the patient is (lactate, vasopressor use, and acidosis), their ventilator settings (PEEP), and their oxygenation (Set FiO2). Interestingly, this was re-enforced in our interviews with clinicians about what clinical data is important to them in their decision making. Clinicians more frequently mentioned indicators of oxygenation (PFR, SpO2), acidosis (ABG), and ventilator settings than chest imaging (CXR and CT scans). This supported our approach to adopt a version of the ARDS Sniffer 2.0 that did not include the chest radiograph data. Conversely, when we surveyed clinicians about the appropriateness of an electronic approach for promoting the EBP of minimizing sedation using GLIA, the clinicians rated the measurability low (below 3). But the research team, who have more expertise with electronic health record data as well as clinical expertise, thought differently. Indeed, ultimately the research team was able to derive an EPM for measuring excessive sedation to a comatose state that was feasible using EHR data and correlated with outcomes.

Nevertheless, the COVID-19 pandemic changed the premise and context behind the planned trial of the ECARDS tool. Prior to the pandemic, we demonstrated sub-optimal recognition and compliance to EBP in patients with ARDS. This provided the practice gap that was to be addressed with this study. With the onset of the pandemic, Montefiore, the study site, was overwhelmed with patients with COVID-19 pneumonia, most of whom had ARDS if they progressed to mechanical ventilation. And because COVID-19 was a new disease without clear treatment at the time, protocols were set up that included EBP in ARDS such as low tidal volume ventilation and proning to guide the management of these patients. That changed the premise of under-recognition and under-utilization of low tidal volume ventilation and proning. Now all COVID-19 patients on mechanical ventilation were assumed to have ARDS. This was supported by our machine learning algorithm, ARDS Sniffer 2.0. Prior to the pandemic, among patients on mechanical ventilation, ARDS Sniffer 2.0 had a sensitivity of 86% with a positive predictive value of 66% for identifying patient who have or will develop ARDS or mortality. Among COVID-19 patients on mechanical ventilation, 70% fulfilled criteria for ARDS. ARDS Sniffer 2.0 still performed well but the prevalence of ARDS was so high that the ARDS Sniffer 2.0 alerted on 75% of the patients with a sensitivity of 94% and a positive predictive value of 92%. This meant that nearly everyone that it alerted on had a high likelihood of having or developing ARDS or death. When the condition is this common, under-recognition is no longer a problem, as the clinicians assume that all of these patients will have ARDS and the use of these machine learning algorithms for identification is not needed. With the emergency protocols, there was much greater standardization of use of low tidal volume ventilation and proning. Specialized proning teams were even developed to help promote proning among clinicians who did not have the expertise or knowledge for proning. While we did demonstrate that other EBPs like daily spontaneous awakening and breathing trials had worse adherence during the pandemic, this is at least partly due to understaffing, and shortages of sedatives requiring use of alternative long acting agents. In addition, with the strain under the pandemic, the hospital wanted additional data on practice variation in ARDS and acute respiratory failure after the pandemic before implementation of ECARDS for a trial.

Conclusions

A multi-modality approach that combines data science with clinician perspectives to build an EHR-based electronic decision support tool in ARDS and acute respiratory failure is feasible and complimentary. A machine learning algorithm using clinical EHR data was developed and found to accurately identify patients with high likelihood of ARDS or death. Interviews with clinicians helped identified those evidence-based practices that they believe to be important and ready for implementation. EHR-based performance measures were developed and validated to measure and track compliance to these evidence-based practices. Informed by clinician feedback and views, identification of ARDS and reporting of compliance to evidence-based practices were incorporated into an electronic dashboard and reporting tool. While the COVID-19 pandemic

prevented the implementation and testing of this tool in the clinical setting, this approach holds promise in the development of electronic clinical decision tools to guide management for other under-diagnosed conditions.

Significance

ARDS is the most severe form of acute respiratory failure with a mortality of 40%. While common, it is only recognized in 1/3 of afflicted patients. Although evidence-based practices exist that have been demonstrated to improve mortality or decrease duration of mechanical ventilation, the under-recognition of ARDS contributes to the low utilization and compliance to these evidence-based practices that is as low as 30%. A long short term memory model that analyzes commonly collected clinical data in the EHR was found to improve detection of ARDS or mortality, capturing 86% of patients with the outcome. This suggests that advanced data science methodology can significantly improve upon clinician recognition of acute conditions. However, while advanced data science techniques can help clinicians in recognizing oft missed conditions in a timely fashion, a systematic appraisal of clinician decision making process, data needs and perspective of the readiness for implementation of evidence-based practices is needed to inform the actions that are needed after identification of the at risk patients.

Implications

The challenge of delivering the right care to the right patient at the right time requires the timely identification of the appropriate patient, determination of evidence-based practices that are appropriate, and direction of clinicians to these evidence-based practices in such a manner that will prompt the timely appropriate management of the patient. The use of EHR data is imperative, since this is now how all clinicians interact with patient data. Advanced data science can help with identification of the right patient at the right time that outperforms clinician recognition. However, data-driven solutions will not be enough to change the behavior of clinicians. An understanding of clinician cognitive decision making and perspectives on the implementability of different clinical practices are key to identifying the right interventions to target and strategies to deliver that information to the clinicians that will facilitate their clinical decision making. Such a multi-modality strategy to electronic clinical decision support tools will be needed in order to improve care and decrease errors in the hospital setting.

LIST OF PUBLICATIONS AND PRODUCTS

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